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Dr. Walter Rogan Oral History 2016

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Interview with Walter Rogan, M.D.

Conducted on October 24, 2016 by Robin Arnette, Ph.D.

National Institute of Environmental Health Sciences

Research Triangle Park, NC

RA: Today is Monday, October the 24th, 2016, and I'm interviewing Walter Rogan, MD, a retired principle investigator in the NIEHS Epidemiology Branch. This interview is part of an effort to collect oral histories of NIH scientists. Good morning.

WR: Good morning.

RA: So, Dr. Rogan, how did you get started in science?

WR: Well, my father was a doctor, and I was always sort of going to go to medical school. In undergraduate, I got mixed up with a biology professor, who was writing parts of environmental impact statements, which were then, there in 1968/'69, not well worked out and institutionalized as they are now. Even big companies like Jersey Central Light and Reserve Mining didn't have in-house capability to write environmental impact statements. They were new things. Earth Day was not even had yet. So, we did mostly surveys of fresh water around what would be industrial discharge sites up in the Great Lakes and Escambia Bay in Florida and Barnegat Bay in New Jersey. It was remarkably exotic and exciting for a college undergraduate to get on an airplane and go someplace and go out in a boat. So that was where the ecology environment side came from.

Then, I went to medical school, and I was in a combined MD-MPH, master of public health, program between UC San Francisco and UC Berkeley. I was a biostatistics major at Berkeley, and that sort of put another little element to it, because it's the sort of quantitative underpinnings of research. It's usual, back in those days it was, for a physician with an interest in research to spend a couple of years at NIH or a couple of years at CDC, somewhere in training. I wanted to do that, and I wanted to go to Bethesda, so I applied there, but I discovered that the environmental one, the environmental institute, which is where my research interest was, was down here. I'd been a coastal guy. I'd grown up in the Philadelphia suburbs and went to medical school in San Francisco, and the notion of coming in from the coast and down to the south was ... But Chapel Hill was charming, even in 19 ... It's hard to imagine now, Chapel Hill in 1976, but Chapel Hill was charming.

Anyway, they were very nice to me down here. Dave Rall called me up personally. I was 26 years old, and an NIH institute director's calling me up and recruiting me. I was the only one of three physicians on campus when I got here: Dave and a guy named Bill [inaudible], whose research was in opossums and he didn't think much about people, and me. I was treated very well and got involved in a research project. At three years, when the staff associate program was up, they said they want me to stay. I was in the middle of working, and so I did. Here I am now, and it's 2016. So that's the whole career, actually. Started in science and finished up.

RA: In what year did you retire from NIEHS?

WR: I retired and then reemployed three years ago, so in 2013. Then, I worked half-time for two years, and then I fully retired this year in June. So now I'm a volunteer. I'm really finishing up a couple of papers that got started when I had a post doc and we didn't finish up.

RA: Tell me about your research. What was your focus while you were here?

WR: I started out doing what has now become children's environmental health, but what Dr. Rall had an interest in was EPA had found PCBs in breast milk. It had been known that there were a variety of pesticide and other contaminants in breast milk for several decades at that point, starting in 1951 with DDT, but the levels were higher than people had thought they would be. EPA came to NIH and said, "What about this?" EPA didn't do much research on people. It fell to us to think primarily about it. There weren't any data. No one had done any studies of what happened if there were PCBs in breast milk and kids were breastfed and along they went. Dave Rall wanted to do a study. I was interested and he was interested in having an intramural, and it was not a very attractive project for extramural scientists because it was very new and there wasn't really a research infrastructure out there to deal with it.

We did that study. We did a study of PCBs and DDT in breast milk and followed kids. It turned out that we and some others found subtle changes in especially motor development as opposed to mental and motor development. You test both in little kids. It's kind of indistinguishable, but mostly motor development. It lasted out to about two years, but it was related to the kids' prenatal exposure through mom's existing body burden rather than through contaminated breast milk. Breast milk didn't seem to affect ... The motor changes didn't seem to occur more in breast-fed kids than could be attributed to their prenatal exposure, and their mental development was faster than non-breast fed kids.

That led to studies in Mexico, where we looked at kids with higher exposures to DDT, because in North Carolina, it looked as if women with higher DDT exposures didn't breastfeed as long, and that, we thought, had something to do with endocrine disruption. So we did a study in Mexico of that and got kind of a partial replication, but it was an interesting study to do. Then, there was an outbreak of PCB poisoning in Taiwan, and that began a long ... There was nobody there with an interest in the kids, so we collaborated with the Taiwanese government. That had to be sort of informal, because there were no diplomatic relations with Taiwan at the time because China objected. The real China. Taiwan claimed that it was not a province of China, it was an independent country, and China claimed that it was a province and no one should deal with it. That was wonderful. Taiwan is the most frequently visited foreign country in my life, and I have made friendships there. I ended up doing a mini sabbatical, a semester living there. It was a wonderful personal and scientific experience.

Those kids whose mothers were clinically poisoned by cooking oil that had been contaminated during manufacturing with PCBs, those kids had a cluster of birth defects. They had short stature. They had odd distribution of pigmentation, genitalia, bridges of the nose, eyelids. They didn't form their teeth or their nails properly. The teeth decayed and chipped. Their nails didn't grow right. They had a global delay in psychomotor development. Their IQ was lower than neighborhood kids who weren't exposed. Their behavior. They had a behavioral deficit that was unusual and we hadn't seen in the North Carolina kids. Those kids were followed by us, to some degree, and also by a local research group that we had established relationships with. That collaboration lasted for decades. The last paper we published out of it was a paper about cancer in the grown-ups that came out now a couple years ago, so the collaboration lasted a few years.

When Ken Olden came, he had an interest in moving the institute in a more clinical direction and also in I believe the old term was minority health. He had an interest in minority health. The institute had supported the development of a drug that lowered blood lead called Succimer. We proposed to Dr. Olden that we do a clinical trial, because lowering blood lead might be a good thing, but it might not be a good thing in the sense of reversing any effect that lead had already had, and it exposed you to the side effects of drug, which you might or might not need. The only thing wrong with you from these low levels of lead that we were going to treat was you'd lost some IQ points, two or three per every 10 micrograms per deciliter of blood lead. So, we wanted to see if we found kids when they were two with these moderately elevated blood leads who otherwise would not have been treated and treated them with this drug to lower their blood lead, would we get their IQ points back?

So, we went to where you might imagine we went. Where was the other centers? Philly, Newark, Baltimore, and Cincinnati. We followed 780 kids, half of whom had gotten Succimer, half of whom got placebo for Succimer. Treated them at around age two, followed them till they were five years old. We lowered their blood leads pretty dramatically, and we changed their IQs not at all. That study ended drug treatment, which had been being promoted as something that you ought to do to these kids. It also stopped the idea of what we call secondary prevention. That is, finding kids who have elevated blood leads and then moving them out of a house or and then doing whatever you were going to do and moved the attention back to primary prevention, not letting them get exposed to lead in the first place.

We didn't anticipate that that would sort of be fallout from that study, but it may turn out, in the very long term, to be the more important contribution that it made, because that sort of search out kids as an indicator of bad housing philosophy had been in place for a long time. Nobody liked it, but people sort of thought, well, it must be a good thing to get kids out of the houses. It turns out it's not as good a thing as keeping them from getting exposed in the first place.

RA: Would you say that study was your most important discovery?

WR: It's not the most cited. The most cited is the stuff in Taiwan about the birth defects in the PCB-exposed kids. That study actually was the basis of, well one of the bases, of the state of California declaring PCBs a known reproductive toxin. I believe that study is probably the most influential. It was a much more simple question to ask and answer and pretty much settled something. Other things don't really settle something, but that study pretty much settled something. It pretty much ended drug treatment of kids with these low levels, relatively low levels. Still too high, but relatively low levels.

RA: What would you consider your most surprising discovery?

WR: I think the most surprising discovery goes back to this idea we had of DDT acting as a weak estrogen and shortening duration of lactation. Without going deep into the weeds of hormones and breastfeeding, you have a lot of estrogen supporting the pregnancy, and then that stops. Then, lactation begins with very little estrogen. Mom has very little estrogen right after birth. The hormones that support lactation, mostly prolactin, act unopposed on the breast. The reason you don't go into full lactation during pregnancy is estrogen inhibits that ability of prolactin to begin the production of milk. If you give somebody a birth control pill postpartum, you decrease their milk supply, especially with the old-fashioned, high-dose estrogen pills. You had to warn women that if they were trying to breastfeed and they were going to take these high-dose pills, that that would be a problem.

We thought that DDT acting as a weak estrogen would interfere with milk production. Thus, women would say, "You know, this kid's not doing well. I'm not making enough milk. I'm going to supplement." Once you start supplementing, breastfeeding ends. That all sounded good as a theory, but it has a lot of steps in it. When you start actually looking at data, it turns out most of the time that complicated theories like that don't end up actually showing up in the data. When we look for that in the North Carolina data, there it was. The women with the highest levels of DDT breastfed a lot shorter than women with ... So that was surprising.

Now, it turns out that, like a lot of other things, we just got lucky or unlucky, whatever you want to call it. We just got lucky on that first data set. It was very clear in those data that higher levels of DDT or DDE, but higher levels of DDT exposure went along with these lower durations of lactation. However, there's been only mixed replication of that, and I'm not sure the biology is true. In our hands, it was true, and in this data, it was true. It was very surprising when a hypothesis as complicated as that one actually turned up in the data.

RA: All right. What about scientific advances that you'd like to see in the next 5 or 10 years in your field?

WR: A lot of the tools and approaches that we've been using to do this kind of work has been the same for the 40 years I've been at this, and it's reasonably simple. You get a cohort of kids, and you measure what they're exposed to in this environmental soup, and then you follow them over time with a bunch of tests. You see how that sort of works out. The difficulty, especially in the United States, is the exposures are largely low to any individual component. The individual cohorts tend to be fairly small, just because they tend to be manageable by one university or a couple of universities. The questions often exceed the lifetime of an investigator. What happens to fertility in kids who are exposed to whatever? What happens to cancer in kids exposed to whatever? The National Children's Study was that writ large. We're going to do 100,000 kids. Even it is sort of small for cancer, and even it is difficult to think about. It's so slow-moving and so difficult to fund that eventually it sort of collapsed under its own weight.

I think we have to move in the direction of much more precision questions and much more scientific tools. We've lately been interested in this idea of endocrine disruption, back to endocrine disruption, where Congress told EPA to figure out endocrine disruptors. Find them out of the mass of chemicals people are exposed to and prevent people from being exposed to them. The Endocrine Society and those groups are saying, "Well, you know, there's lower sperm counts and there's infertility and there's breast cancer, and these things are due to endocrine disruption in early life." Well, that's a big gap between laboratory studies looking at occupancy of a human estrogen receptor in a cell system and infertility over here, which may or may not have anything to do with estrogen exposure.

We've been doing a study with Children's Hospital in Philadelphia where we have a relatively small number of kids, and we've developed tests that are very sensitive specifically to estrogen exposure. Kids have estrogen-responsive tissues. Breast tissue responsive to estrogen in the kid is the same as it is in the adult. The lining of the uterus has estrogen receptors on it, and it's the same in a baby girl as it is in a grown-up. What you don't have is the estrogen. It's not that you don't have the uterus.

We set up a study. Then, you need an endocrine disruptor, right? You need exposure to an estrogen. In the United States, a fair chunk of kids are exposed to soy formula. They have soy formula. Soy formula has soy beans. Soy beans have estrogen in them, and everybody knows that. That's not a secret, that there's estrogens in soy beans. Plant estrogens. Genistein is the most common one. We've done a study where we have used our estrogen-detecting tools, the size of the uterus detected with ultrasound, the characteristics of a test a lot like a pap smear that looks at estrogen response in cells of the vagina in girls and the very end of the urethra in boys, which are the same tissue in the embryo. The synthesis of sex hormones, which kids do briefly before their second birthday. We had kids who had soy formula from when they were born and kids who have cow milk formula and breast feeders. We're still finishing up the analysis of that big study, but along the way, we collaborated with Jack Taylor to use a new tool, epigenetic alterations in cells. Sophia Harlid in Jack's group showed that soy-fed girls had these methylation changes in the cells of their vagina more often than the cow-milk-fed formula girls did.

That's a signal that there's enough of these plant estrogens to produce an estrogen response in the baby. It doesn't say that something bad is going to happen, but it says there's enough of this plant estrogen that the cells are responding as if they've seen something that's active. That's often the question in environmental health, not whether exposure has occurred or not. You know exposure has occurred. The question is whether you're responding to that exposure in some way.

I think that the advance I'd like to see is precision questions and precision answers based on these short causal chain biological reasoning rather than big data sets, low exposures, insensitive markers, and sort of surveying the data to see what the data tell you rather than entering the data with a specific hypothesis about what you think is happening. I think we're drifting in children's environmental health, and we have to come back to the roots. That's what old people say, in general, so there you go.

RA: Name a skill that you think every scientist should possess.

WR: I don't know if it's a skill as much a characteristic, but curiosity. The thing I have noticed over the years is that people who do well are curious and they're persistent. If you're persistent but not curious, you're not good at figuring out questions. If you're curious but not persistent, you can figure out questions, but you can't answer them. Those two things are what I've seen. I don't think you can be a scientist without those.

RA: If you had not become a scientist, what career?

WR: I would have practiced medicine.

RA: Would you be an OB/GYN?

WR: No, I'd probably be a pediatrician.

RA: Really? Okay.

WR: Although, I don't know. The branch occurred so early that it's hard to know. It's hard to know, but I don't think I would have done OB /GYN if I was going to. I would have done pediatrics or I would have done adult internal medicine. I don't think I would have been a surgeon.

RA: All right. For our last question, looking back over your career here at NIEHS, how has this institute given you an advantage or been better for you than being at another institute or maybe at an academic institution?

WR: Nothing I've done would have been possible outside of a government agency, either NIH or CDC or EPA. These things, doing collaborative projects with foreign governments, doing very new stuff, doing big clinical trials where the research infrastructure is ... All these things are very, very difficult to support with a grant mechanism. My career has been very much a government scientist career. I came to NIH with an interest in environmental health, so there, we're done, in one sense. However, I was welcomed here in way that astonished me, even at the time and, in retrospect, really astonishes me. I was one of the people who was asked to speak on the tape that they made when Dave Rall died. What I talk about is the degree of respect and collegiality I was offered as a 27-year-old. I was valued as a scientist and encouraged to build a research program in environmental epidemiology, or epidemiology let's call it.

There wasn't one here when I got here. It was me. That, even then, was unimaginable and now is even more unimaginable. I just can't see that happening now, but for me, it was great. I overcame my bi-coastal prejudice about where it was possible to live. Epidemiology, at its peak, got up to seven PIs and 10 PIs, I guess. Now, we're sort of in a period of reformation. I'm retired. Alan and Dale and Donna are in their 60s. Stephanie will turn 60 this year, I think. So we're getting older. There's new tenure-track people, and it'll be very different after that.

This period of growth, being here for this period of growth and support and support of my own research has been very, very unusual, I think. The career, as it was, could not have been done. It's uniquely NIEHS. It couldn't have been done anyplace else.

RA: Great. Do you have anything else that you'd like to add?

WR: No, that's pretty much it. You know, the institute was only seven years old when I got ... It had really become an institute in sort of '69. Everybody was very young. Dave was in his 40s. Dave Hall, who I worked for directly, was in his, actually, late 30s. I was 35 when I was epidemiology branch chief. Now, you're just starting when you're 35.

RA: All right. Well, Dr. Rogan, thank you so much for your time.

WR: Well, thank you.

End of transcript